09/404,448.

02-09-05

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I hereby certify that this correspondence is being deposited with the U.S. Postal Service as Express Mail, Airbill No. EV 307 814 144 U.S. in an envelope addressed to: MS Post Issue, Commissioner for Patents, P.O. Box 1450 Alexandria, VA 22313-1450, on the date shown below

Dated: 2/7/05

Signature: Von Giufffida)

Docket No.: 60693US (49163) (PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Letters Patent of: Barry J. Byrne et al.

Patent No.: 6,783,972 B |

Issued: August 31, 2004

For: METHODS FOR LARGE-SCALE

PRODUCTION OF RECOMBINANT AAV

VECTORS

REQUEST FOR CERTIFICATE OF CORRECTION PURSUANT TO 37 CFR 1.323

MS Post Issue Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450 Certificate
FEB 1 6 2005
of Correction

Dear Sir:

Upon reviewing the above-identified patent, Patentee noted an error concerning an omission of an Assignee which should be added and/or corrected.

Applicants inadvertently failed to request listing of the co-assignee, The Johns Hopkins University, when submiting the payment of Issue Fee. Included with this request are copies of the recorded assignment documents clearly showing that The Johns Hopkins University and University of Florida Research Foundation are co-assignees. Should a fee be required under 37 CFR §120(a), please charge our Deposit Account No. 04-1105 in the amount of \$100.00.

The omission now sought to be corrected is our inadvertent error, the correction of which does not involve new matter or require reexamination.

02/11/2005 SSITHIB2 00000129 041105 6783972 01 FC:1811 100.00 DA Patent No.: 6,783,972 2 Docket No.: 60693US (49163)

Transmitted herewith is a proposed Certificate of Correction effecting such amendment. Patentee respectfully solicits the granting of the requested Certificate of Correction.

The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 04-1105, under Order No. 60693US (49163).

Dated

Respectfully submitted,

Barbara S. Kitchell

Registration No.: 33,928 EDWARDS & ANGELL, LLP

P.O. Box 55874

Boston, Massachusetts 02205

(203) 353-6848

Attorney for Applicant



PTO/SB/44 (04-04)
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ork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.
(Also Form PTO-1050)

UNITED STATES PATENT AND TRADEMARK OFFICE CERTIFICATE OF CORRECTION

PATENT NO.

6.783.972 BI

DATED

August 31, 2004

INVENTOR(S) :

Barry J. Byrne et al.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

ASSIGNEE: Please add the following additional Assignee:

THE JOHNS HOPKINS UNIVERSITY BALTIMORE, MD (US)

MAILING ADDRESS OF SENDER: Barbara S. Kitchell EDWARDS & ANGELL, LLP P.O. Box 55874 Boston, Massachusetts 02205

PATENT NO. 6,783,972

No. of additional copies _





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ASSISTANT SECRETARY AND COMMISSIONER OF PATENTS AND TRADEMARKS Washington, D.C. 20231

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WILLIAMS, MORGAN, & AMERSON, P.C. DAVID W. HIBLER 7676 HILLMONT, SUITE 250 HOUSTON, TEXAS 77040



APR 2 0 2000

WILLIAMS, MORGAN & AMERSON

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RECORDATION DATE: 01/10/2000

REEL/FRAME: 010530/0762

NUMBER OF PAGES: 4

BRIEF: ASSIGNMENT OF ASSIGNOR'S INTEREST (SEE DOCUMENT FOR DETAILS).

ASSIGNOR:

BYRNE, BARRY J.

DOC DATE: 12/16/1999

ASSIGNOR:

MUZYCZKA, NICHOLAS

DOC DATE: 12/16/1999

ASSIGNOR:

ZOLOTUKHIN, SERGEI

DOC DATE: 12/16/1999

ASSIGNEE:

FLORIDA, UNIVERSITY OF 1938 W. UNIVERSITY AVENUE GAINESVILLE, FLORIDA 32603

SERIAL NUMBER: 09404448

IFFUCINIES FOR THE TREE BY AND A SANDON

PATENT NUMBER:

FILING DATE: 09/22/1999 ISSUE DATE:

នៃទី១១១១ភ<u>ិ</u>

ASSIGNMENT

FOR GOOD AND VALUABLE CONSIDERATION, the receipt, sufficiency and adequacy of which are hereby acknowledged, the undersigned, do hereby:

SELL, ASSIGN AND TRANSFER to University of Florida (the "Assignee"), having a place of business at 1938 W. University Avenue, Gainesville, Florida, 32603, our entire right, title and interest for the United States and all foreign countries in and to any and all improvements which are disclosed in the application for United States Letters Patent, Serial No. 09/404,448 which has been filed on September 22, 1999 and is entitled "METHODS FOR LARGE-SCALE PRODUCTION OF RECOMBINANT AAV VECTORS", such application and all divisional, continuing, substitute, renewal, reissue and all other applications for patent which have been or shall be filed in the United States and all foreign countries on any of such improvements; all original and reissued patents which have been or shall be issued in the United States and all foreign countries on such improvements; and specifically including the right to file foreign applications under the provisions of any convention or treaty and claim priority based on such application in the United States;

AUTHORIZE AND REQUEST the issuing authority to issue any and all United States and foreign patents granted on such improvements to the Assignee;

WARRANT AND COVENANT that no assignment, grant, mortgage, license or other agreement affecting the rights and property herein conveyed has been or will be made to others by the undersigned, and that the full right to convey the same as herein expressed is possessed by the undersigned;

COVENANT, when requested and at the expense of the Assignee, to carry out in good faith the intent and purpose of this assignment, the undersigned will execute all divisional, continuing, substitute, renewal, reissue, and all other patent applications on any and all such improvements; execute all rightful oaths, declarations, assignments, powers of attorney and other papers; communicate to the Assignee all facts known to the undersigned relating to such improvements and the history thereof; and generally do everything possible which the Assignee shall consider desirable for vesting title to such improvements in the Assignee, and for securing, maintaining and enforcing proper patent protection for such improvements;

TO BE BINDING on the heirs, assigns, representatives and successors of the undersigned and extend to the successors, assigns and nominees of the Assignee. Date: 12/16/99 Signature: STATE OF FLORIDA COUNTY OF Alachna BEFORE ME, the undersigned authority, on this ______ day of ______, 1999, personally appeared Barry J. Byrne, known to me to be the person whose name is subscribed to the foregoing instrument and acknowledged to me that he executed the same of his own free will for the purposes and consideration therein expressed. Notary or Consular Officer Vicky R. Parrott [SEAL] MY COMMISSION # CC864994 EXPIRES August 22, 2003 Date: Name: Nicholas Muzyczl STATE OF FLORIDA COUNTY OF BEFORE ME, the undersigned authority, on this <u>\$\lambda\leq\$</u> day of <u>Dec.</u>, 1999, personally appeared Nicholas Muzyczka, known to me to be the person whose name is subscribed to the foregoing instrument and acknowledged to me that he executed the same of his own free will for the purposes and consideration therein expressed. Notary or Consular Officer

[SEAL]

	(
Signature:	Date:	12/16/99
STATE OF FLORIDA) COUNTY OF Alaehua)	SS.	
BEFORE ME, the undersign personally appeared Sergei Zolotukhin to the foregoing instrument and acknowill for the purposes and consideration	n, known to me to be the person owledged to me that he execute the therein expressed.	ed the same of his own free
[SEAL]		Vicky R. Parrott MISSION # CC364994 EXPIRES August 22, 2003 THRU TROY FAIN INSURANCE INC

010530/0762 PAGE 2

ALLYSON PURNELL, EXAMINER ASSIGNMENT DIVISION OFFICE OF PUBLIC RECORDS

02-10-2000

FORM PTO-1595 (Rev. 6-93) RE OMB No. 0651-0011 (exp. 4/94)	U.S. Department of Commerce
1. Name of conveying party(ies): Barry J. Byrne, Nicholas Muzyczka ar Zolotukhin Additional name(s) of conveying party(ies) attached? Yes 3. Nature of conveyance: Assignment Merger Security Agreement Change of Nar Other Execution Date: December 16, 1999	Street Address: 1938 W. University Avenue City: Gainesville State: Florida zip: 32603
4. Application number(s) or registration number(s): If this document is being filed together with a new application, the A. Patent Application No.(s): 09/404,448	the execution date of the application is: B. Patent No.(s):
Addition Name and address of party to whom correspondence concerning document should be mailed:	onal numbers attached? Yes No 6. Total number of applications and patents involved: 1
Name: David W. Hibler Williams, Morgan & Amerson, P.C. 7676 Hillmont, Suite 250 City: Houston State: Texas Zip: 77	7. Total fee (37 C.F.R. 3.41) \$\sum \sum \subseteq \text{Enclosed}\$ Authorized to be charged to deposit account if check insufficient or inadvertently omitted
· · · · · · · · · · · · · · · · · · ·	8. Deposit account number: 50-0786/4300.012100 (Attach duplicate copy of this page if paying by deposit account)
Statement and signature.	on is true and correct and any attached copy is a true copy of the original document. David W. Helen 1/6/2000
Name of Person Signing, Reg. No. 41,071	Signature Date Total number of pages including cover sheet, attachments and documents: 7 recorded with required cover sheet information to:
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APRIL 15, 2000

DAVID W. HIBLER

HOUSTON, TX 77040

7676 HILLMONT, SUITE 250



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Williams, Morgan & Amerson

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RECORDATION DATE: 01/10/2000

REEL/FRAME: 010530/0775

NUMBER OF PAGES: 3

BRIEF: ASSIGNMENT OF ASSIGNOR'S INTEREST (SEE DOCUMENT FOR DETAILS).

ASSIGNOR:

CONWAY, JAMES E.

DOC DATE: 11/24/1999

ASSIGNOR:

HAYWARD, GARY S.

DOC DATE: 11/24/1999

ASSIGNEE:

JOHNS HOPKINS UNIVERSITY, THE 111 MARKET PLACE, SUITE 906 BALTIMORE, MARYLAND 21202

SERIAL NUMBER: 09404448

PATENT NUMBER:

FILING DATE: 09/22/1999

ISSUE DATE:

SEDLEY PYNE, PARALEGAL ASSIGNMENT DIVISION OFFICE OF PUBLIC RECORDS

ASSIGNMENT

FOR GOOD AND VALUABLE CONSIDERATION, the receipt, sufficiency and adequacy of which are hereby acknowledged, the undersigned, does hereby:

SELL, ASSIGN AND TRANSFER to The Johns Hopkins University (the "Assignee"), having a place of business at 111 Market Place, Suite 906, Baltimore, Maryland 21202, my entire right, title and interest for the United States and all foreign countries in and to any and all improvements which are disclosed in the application for United States Letters Patent, Serial No. 09/404,448 which has been filed on September 22, 1999 and is entitled "METHODS FOR LARGE-SCALE PRODUCTION OF RECOMBINANT AAV VECTORS", such application and all divisional, continuing, substitute, renewal, reissue and all other applications for patent which have been or shall be filed in the United States and all foreign countries on any of such improvements; all original and reissued patents which have been or shall be issued in the United States and all foreign countries on such improvements; and specifically including the right to file foreign applications under the provisions of any convention or treaty and claim priority based on such application in the United States;

AUTHORIZE AND REQUEST the issuing authority to issue any and all United States and foreign patents granted on such improvements to the Assignee;

WARRANT AND COVENANT that no assignment, grant, mortgage, license or other agreement affecting the rights and property herein conveyed has been or will be made to others by the undersigned, and that the full right to convey the same as herein expressed is possessed by the undersigned;

COVENANT, when requested and at the expense of the Assignee, to carry out in good faith the intent and purpose of this assignment, the undersigned will execute all divisional, continuing, substitute, renewal, reissue, and all other patent applications on any and all such improvements; execute all rightful oaths, declarations, assignments, powers of attorney and other papers; communicate to the Assignee all facts known to the undersigned relating to such improvements and the history thereof; and generally do everything possible which the Assignee shall consider desirable for vesting title to such improvements in the Assignee, and for securing, maintaining and enforcing proper patent protection for such improvements;

TO BE BINDING on the heirs, assigns, representatives and successors of the undersigned and extend to the successors, assigns and nominees of the Assignee.

Signature: Add Continued	C Date: 17 19 1999
Name: James E. Conway	Mild Cenway Wovember 24, 1899
STATE OF MARYLAND)
COUNTY OF <u>Cecil</u> Cecil) ss.)
BEFORE ME, the undersign personally appeared James E. Conwa	ned authority, on this 24 day of Movembee, 1999, y, known to me to be the person whose name is subscribed owledged to me that he executed the same of his own free
	Elizabeth W. Morris Notary or Consular Officer
	Notary or Consular Officer
[SEAL]	ULIZABETH H. NORRIS NOTARY PUBLIC COMMISSION EXPIRES 3/1/02
Signature:Name: Gary S. Hayward	Date: 1 24 1997
STATE OF MARYLAND COUNTY OF Balhnore)) ss.)
personally appeared Gary S. Hayward	ned authority, on this <u>Juli</u> day of <u>November</u> , 1999, d, known to me to be the person whose name is subscribed owledged to me that he executed the same of his own free in therein expressed.
	Notary or Consular Officer J
[QEAT]	-
[SEAL]	my commission expires billion

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02-10-2000



U.S. Department of Commerce

OMB No. 0651-0011 (exp. 4/94) [Rev. 6-93) [OMB No. 0651-0011 (exp. 4/94)] [OMB No. 0651-0011 (exp. 4/94)]	1264876 Patent and Trademark Office			
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James E. Conway and Gary S. Hayward Additional name(s) of conveying party(ies) attached? Yes No 3. Nature of conveyance: Assignment Merger Security Agreement Change of Name Other Execution Date: November 24, 1999	Name: The Johns Hopkins University Street Address: 111 Market Place, Suite 906 City: Baltimore State: Maryland zip: 21202 Additional name(s) & address(es) attached? Yes No			
 Application number(s) or registration number(s): If this document is being filed together with a new application, the execution data. A. Patent Application No.(s): 09/404,448 	B. Patent No.(s):			
Additional numbers attached? Yes No				
 Name and address of party to whom correspondence concerning document should be mailed: 	6. Total number of applications and patents involved: 1			
Name: David W. Hibler Williams, Morgan & Amerson, P.C. 7676 Hillmont, Suite 250 City: Houston State: Texas zip: 77040	7. Total fee (37 C.F.R. 3.41) \$\square\$ Enclosed \$\square\$ Authorized to be charged to deposit account if check insufficient or inadvertently omitted 8. Deposit account number: 50-0786/4300.012100			
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9. Statement and signature.				
To the best of my knowledge and belief, the foregoing information is true and con				
	David W Zleken 1/6/2000			
Name of Person Signing, Reg. No. 41,071	Signature Date			
Mail documents to be recorded with reco	Total number of pages including cover sheet, attachments and documents:			
Mail documents to be recorded with required cover sheet information to: Commissioner of Patents and Trademarks. Box Assignment				

Washington, D.C. 20231

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January 6, 2000

Date

avid W. Debley David W. Hibler

02/10/2000 DHGUYEN 00000022 09404448

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APRIL 19, 2002

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WILLIAMS, MORGAN & AMERSON, P.C. MARK D. MOORE 7676 HILLMONT, SUITE 250 HOUSTON, TEXAS 77040 Chief Financial Officer and Chief Administrative Officer Washington, DC 20231 www.uspto.gov



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RECORDATION DATE: 02/19/2002

REEL/FRAME: 012600/0400

NUMBER OF PAGES: 3

BRIEF: ASSIGNMENT OF ASSIGNOR'S INTEREST (SEE DOCUMENT FOR DETAILS).

ASSIGNOR:

FLORIDA, UNIVERSITY OF

DOC DATE: 12/12/2001

ASSIGNEE:

UNIVERSITY OF FLORIDA RESEARCH FOUNDATION 223 GRINTER HALL GAINESVILLE, FLORIDA 32611

SERIAL NUMBER: 09404448

PATENT NUMBER:

FILING DATE: 09/22/1999

ISSUE DATE:

TONYA LEE, EXAMINER ASSIGNMENT DIVISION OFFICE OF PUBLIC RECORDS



FORM PTO-1595 (Rev. 6-93)

02-27-2002



101996745 **PATENTS ONLY** U.S. Department of Commerce

OMB No. 0651-0011 (exp. 4/94)	PATENTS ONLY	Patent and Trademark O
To the Honorable Commissioner of Patents at	nd Trademarks: Please record the attached o	original document or copy thereof.
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University of Florida Additional name(s) of conveying party(ies) attached? Yes		sity of Florida Research Foundation
3. Nature of conveyance: Assignment Merger	Internal Address: 2	223 Grinter Hall
Security Agreement Change of Name Other	Street Address:	
Execution Date: December 12, 2001	City: Gainesvi	lle State: FL Zip: 32611
	Additional name(s) &	address(es) attached? Yes X
4. Application number(s) or registration number(s):		
If this document is being filed together with a new application, the	execution date of the application is:	
A. Patent Application No.(s):	B. Patent No.(s):	
09/404,448		
Additiona	ul numbers attached? Yes No	
Name and address of party to whom correspondence concerning document should be mailed:	6. Total number of ap	plications and patents involved: 1
Name: Mark D. Moore Williams, Morgan & Amerson, P.C. 7676 Hillmont, Suite 250	Enclosed	be charged to deposit account inadvertently omitted
City: Houston State: Texas Zip: 7704	o. Deposit account nui	mber: 50-0786/4300.012100 opy of this page if paying by deposit according
DO N	NOT USE THIS SPACE	
9. Statement and signature.		
To the best of my knowledge and belief, the foregoing information i	is true and correct and any attached copy	·
MARK D. MOORE Name of Person Signing, Reg. No. 42,903		-
Traine of Leison of Bring, Ireg. 140. 42,503	Mark D. Mark D	Moore Date of
02 GTON11 00000024 09404448 Commissioner of P	corded with required cover sheet information to: Patents and Trademarks, Box Assignment Vashington, D.C. 20231	a a series and a comment
CE	ERTIFICATE OF MAILING 37 C.F.R 1.8	
I hereby certify that this correspond First Class Mail in an envelope a Trademarks, Washington, D.C. 202	dence is being deposited with the U.S. Faddressed to: Assistant Commissioner	Postal Service as of Patents and

February 1, 2002 Date

Mark D. Moore

ASSIGNMENT FROM THE UNIVERSITY OF FLORIDA

TO THE

UNIVERSITY OF FLORIDA RESEARCH FOUNDATION, INC.

In consideration of one dollar (\$1.00) and other good and valuable consideration, the UNIVERSITY OF FLORIDA, existing by virtue of the laws of the State of Florida, and having an office at 223 Grinter Hall, Gainesville, Florida 32611, sells and assigns to the UNIVERSITY OF FLORIDA RESEARCH FOUNDATION, INCORPORATED, a Florida not for profit corporation, having its office at 223 Grinter Hall, Gainesville, Florida 32611, its successors and assigns, its entire right, title and interest throughout the world in and to the improvements in :

A Scaleable Method for Production of Recombinant AAV, UF#-10014, U.S. Serial No. 09/404,448, filed 4/21/99, created by Barry J. Byrne, Serge Zolotukhin, Nicholas Muzyczka, James E. Conway, and Gary Hayward, inventors;

and in and to said application and all patents (foreign and domestic) which may be granted therefore and thereon, and all divisions, continuations and extensions thereof (foreign and domestic), subject to performance by the UNIVERSITY OF FLORIDA RESEARCH FOUNDATION, INCORPORATED, of the obligations of the UNIVERSITY OF FLORIDA under the UNIVERSITY OF FLORIDA'S Patent Policy with regard to the above-described invention, and the UNIVERSITY OF FLORIDA covenants that it has full right to so sell and assign; and it authorizes and requests the Commissioner of Patents and Trademarks to issue all patents on said improvements or resulting therefrom to said UNIVERSITY OF FLORIDA RESEARCH FOUNDATION, INCORPORATED, as assignee; and it agrees that it communicate to said UNIVERSITY OF FLORIDA RESEARCH FOUNDATION, INCORPORATED, or its representatives any facts known to it respecting said improvements, and testify in any legal proceedings, sign all lawful papers, execute all divisional, continuing and reissue applications, make all rightful oaths and generally do everything possible to aid said UNIVERSITY OF FLORIDA RESEARCH FOUNDATION, INCORPORATED, its successors, assigns and nominees, to obtain and enforce proper protection for said improvements in all countries.

Executed this 12 day of December, 2001.

UNIVERSITY OF FLORIDA

CHARLES E. YOUNG, PRESIDENT

Assignment from UF to UFRFI Page two of two

COUNTY OF ALACHUA STATE OF FLORIDA

Accepted by UNIVERSITY OF FLORIDA RESEARCH FOUNDATION, INC.

By: Winfred M Ohlyon

Winfred Phillips, Vice President

Attest:

Kathleen a. Wilson

(12) United States Patent

Byrne et al.

(10) Patent No.:

US 6,783,972 B1

(45) Date of Patent:

Aug. 31, 2004

METHODS FOR LARGE-SCALE PRODUCTION OF RECOMBINANT AAV VECTORS

(75) Inventors: Barry J. Byrne, Gainesville, FL (US); James E. Conway, Elkton, MD (US); Gary S. Hayward, Towson, MD (US); Nicholas Muzyzcka, Gainesville, FL (US); Sergei Zolotukhin, Gainesville, FL (US)

Assignee: University of Florida Research (73)Foundation, Gainesville, FL (US)

Subject to any disclaimer, the term of this (*) Notice: patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: 09/404,448

Sep. 22, 1999 (22) Filed:

Related U.S. Application Data

Provisional application No. 60/101,507, filed on Sep. 22,

Int. Cl.⁷ C12N 7/01; C12N 15/09; C12N 15/00; C12P 21/06; C07H 21/04

435/325; 435/456; 435/69.1; 536/23.1;

(58) 435/320.1, 456, 69.1; 536/23.1; 514/44

(56)References Cited

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ABSTRACT

Disclosed are HSV-1 amplicons that supply all necessary helper functions required for rAAV packaging and methods for their use. These HSV-1 amplicons have been shown to be capable of rescuing and replicating all forms of rAAV genomes including rAAV genomes introduced into cells by infection of rAAV virions, rAAV genomes transfected into cells on plasmids or proviral rAAV genomes integrated into cellular chromosomal DNA. Also provided are methods for preparing high-titer rAAV vector compositions suitable for gene therapy and the delivery of exogenous polynucleotides to selected host cells.

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